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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,066	09/24/2004	Ulrich Abel	12874-00001-US	1371

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EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,066	ABEL ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-14 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-14 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims pending 1-14.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim.

The claims recites "a preparation for the treatment."

The examiner has treated them to be a method of treating and has examined them accordingly.

Claims 1-10 are also rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim.

The various terms such as residues, and inclusion compounds is not clear as to what is included and what is not. See page 7 of claim 1.

The term residue can read on any group including just H.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recites in the definition of the various R variables the heterocyclo and heteroaryls, heterocyloalkyl,, alkylheteroaryl (all group with the hetero encompassed in it) but the specification s do not have any definition of what these group are.

Also in various places the claims recite forming a ring with N , O or S , but there is no definitions as to which groups are encompassed by this , in the specification.

Also the term residues , is not defined. The various residues can also read on H.

There is also no description of the " further agents for tumor treatment" limitation of claim 10.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for formel, does not reasonably provide enablement for various derivatives of the compounds and method of treatment of tumors, parasites, immunosuppressant, neurodermitis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary

skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds.

2) The nature of the invention: The invention is a (highly) substituted spiro compound that is useful to treat tumors, parasites, immunosuppressant, , neurodermitis.

3) The state of the prior art: The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses a hydrogen changes the properties altogether. A good example is a theophylline verses caffeine . They differ by just a methyl group but one of them has a pharmaceutical use as a broncodialator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face..

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodialator and they differ only by a methyl group.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no examples with the R being the various groups and also there is no data provided to show that these compounds do indeed treat tumors, parasites, immunosuppressant, , neurodermitis . The only data provided is for some tumor activity against a few cell line, see page 21 of the specifications. About 29 compounds were shown to have some IC70 activity , which ranged from .0030 to about .3000. This does no tindicate that the compounds can treat tumors, parasites, are immunosuppressant or that they can treat neurodermitis.

7) The existence of working examples: The instant specification does not have any working examples. There is no in vivo data , nor any population data that it does in fact treat the above mentioned diseases and disorders.
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention. In view of the high unpredictability and the fact that the specifications have not clearly defined and described some of the substitutions and with such vague definitions and no data , it is clear that the applicants have enable the scope of the claimed compounds and also have not enabled the method of treating the various diseases.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1- 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4584377, 4673678, 5166208, and

Cyclodextrin solubilization of the antibacterial agents.... Matt Duan et al, or/and Reaction of β- Cyclodextrin with N-2,3-epoxypropylphthalimide. Preparation, Characterisation and Study of a New Substituted Cycloheptaamylose. Effect on Water Solubility of drugs by Raquel Delgado et al.and or Releases of Testoseterone from an osmotic pump tablet utilizing (SBE)7m-β-cyclodextrin as both a solubilizing and an osmotic pump agent by Kazuto Okimoto et al.

Applicants compounds are drawn to Formel derivatives which are more soluble and are effective in treating tumors , as immunosuppressants, treat parasites and neurodermitis.
The scope of the derivatives is vary large and covers many compounds.

Determination of the scope and content of the prior art (MPEP §2141.01)

US 4584377, 4673678 and 5166208 all teach the Fredericamycin derivatives and that they have antitumor activity and antibacterial activity. Yokoi et al '377 teaches the compounds that read on the instant application.. So does Misra'678.

Misra '678 also teaches the water soluble salts sodium, potassium and lithium salts and also the fact that sugar s would form more soluble compounds and (polyethylene glycols such as propylene glycol, glycerol sorbitol) . Thus sugars and also the salts make the compound more soluble and much more suitable as carriers of the active ingredient. See columns 17 and 18 of the reference.

These reference also teach using these compounds as antitumor agents. Thus if the compounds are made more soluble then the bioavailability would obviously increase since the amount will increase and hence the effectiveness of the compound should also increase.

Cyclodextrin solubilization of the antibacterial agents.... Matt Duan et al, or/and Reaction of β- Cyclodextrin with N-2,3-epoxypropylphthalimide. Preparation, Characterisation and Study of a New Substituted Cycloheptaamylose. Effect on Water Solubility of drugs by Raquel Delgado et al.and or releases of testoseterone from an osmotic pump tablet utilizing (SBE)7m-β-cyclodextrin as both a solubilizing and an osmotic pump agent by Kazuto Okimoto et al. All these reference teach the inclusion of the cyclodextrin to make some drugs more soluble and hence more bioavalable.See whole doment Kazuto , Delgado et al and also Duan. "They explain that in the hydrated state the cavity formed in the cyclic cyclodextrin is filled with water but which can be replaced by non-polar molecules(the active drug) with a corresponding gain in energy. The structure and thermodynamics of these host-guest complexes were found to determine the particular properties of solubility or accessibility. This type of compound may be used in drug delivery systems." See Delgado page 205.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The compounds of the invention are the derivatives of the Fredericamycin and the cyclodextrin inclusive compound.

The prior art does not specifically disclose the cylodextrin inclusion fo fredericamycin.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The various non-patent literature cited above disclose other nonpolar drugs and also the state of the art as to how they can be made more soluble and bioavailable.

The US patents all disclose the Fredericamycin . thus with the knowledge of the state of the art at the time of the invention, one of skill in the art would be motivated to make the more

soluble and bioavailable salts and sugar residue and also the cyclodextrin complexs as given in the claims.

Conclusion

The claims 1-14 are not found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday,9:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rita J. Desai
Primary Examiner
Art Unit 1625

R.D.
April 13, 2006